

## SEQUENCE LISTING

## (1) GENERAL INFORMATION:

- (i) APPLICANT: Madison, Edwin L
- (ii) TITLE OF INVENTION: TISSUE TYPE PLASMINOGEN ACTIVATOR (t-PA)  
VARIANTS HAVING ZYMOGEN CHARACTERISTICS: COMPOSITIONS AND  
METHODS OF USE
- (iii) NUMBER OF SEQUENCES: 1
- (iv) CORRESPONDENCE ADDRESS:  
(A) ADDRESSEE: McDonnell Boehnen Hulbert & Berghoff  
(B) STREET: 300 South Wacker Drive, 32nd Floor  
(C) CITY: Chicago  
(D) STATE: IL  
(E) COUNTRY: USA  
(F) ZIP: 60606
- (v) COMPUTER READABLE FORM:  
(A) MEDIUM TYPE: Floppy disk  
(B) COMPUTER: IBM PC compatible  
(C) OPERATING SYSTEM: PC-DOS/MS-DOS  
(D) SOFTWARE: Patent In Release #1.0, Version #1.30
- (vi) CURRENT APPLICATION DATA:  
(A) APPLICATION NUMBER:  
(B) FILING DATE:  
(C) CLASSIFICATION:
- (viii) ATTORNEY/AGENT INFORMATION:  
(A) NAME: Zimmerman, Roger P  
(B) REGISTRATION NUMBER: 38,670  
(C) REFERENCE/DOCKET NUMBER: 97,707
- (ix) TELECOMMUNICATION INFORMATION:  
(A) TELEPHONE: 312-913-0001  
(B) TELEFAX: 312-913-0002

## (2) INFORMATION FOR SEQ ID NO:1:

- (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 527 amino acids  
(B) TYPE: amino acid  
(C) STRANDEDNESS: not relevant  
(D) TOPOLOGY: not relevant
- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- (iv) ANTI-SENSE: NO
- (vi) ORIGINAL SOURCE:  
(A) ORGANISM: Homo sapiens

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

Ser Tyr Gln Val Ile Cys Arg Asp Glu Lys Thr Gln Met Ile Tyr Gln  
 1 5 10 15  
 Gln His Gln Ser Trp Leu Arg Pro Val Leu Arg Ser Asn Arg Val Glu  
 20 25 30  
 Tyr Cys Trp Cys Asn Ser Gly Arg Ala Gln Cys His Ser Val Pro Val  
 35 40 45  
 Lys Ser Cys Ser Glu Pro Arg Cys Phe Asn Gly Gly Thr Cys Gln Gln  
 50 55 60  
 Ala Leu Tyr Phe Ser Asp Phe Val Cys Gln Cys Pro Glu Gly Phe Ala  
 65 70 75 80  
 Gly Lys Cys Cys Glu Ile Asp Thr Arg Ala Thr Cys Tyr Glu Asp Gln  
 85 90 95  
 Gly Ile Ser Tyr Arg Gly Thr Trp Ser Thr Ala Glu Ser Gly Ala Glu  
 100 105 110  
 Cys Thr Asn Trp Asn Ser Ser Ala Leu Ala Gln Lys Pro Tyr Ser Gly  
 115 120 125  
 Arg Arg Pro Asp Ala Ile Arg Leu Gly Leu Gly Asn His Asn Tyr Cys  
 130 135 140  
 Arg Asn Pro Asp Arg Asp Ser Lys Pro Trp Cys Tyr Val Phe Lys Ala  
 145 150 155 160  
 Gly Lys Tyr Ser Ser Glu Phe Cys Ser Thr Pro Ala Cys Ser Glu Gly  
 165 170 175  
 Asn Ser Asp Cys Tyr Phe Gly Asn Gly Ser Ala Tyr Arg Gly Thr His  
 180 185 190  
 Ser Leu Thr Glu Ser Gly Ala Ser Cys Leu Pro Trp Asn Ser Met Ile  
 195 200 205  
 Leu Ile Gly Lys Val Tyr Thr Ala Gln Asn Pro Ser Ala Gln Ala Leu  
 210 215 220  
 Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Gly Asp Ala Lys  
 225 230 235 240  
 Pro Trp Cys His Val Leu Lys Asn Arg Arg Leu Thr Trp Glu Tyr Cys  
 245 250 255  
 Asp Val Pro Ser Cys Ser Thr Cys Gly Leu Arg Gln Tyr Ser Gln Pro  
 260 265 270  
 Gln Phe Glu Ile Lys Gly Gly Leu Phe Ala Asp Ile Ala Ser His Pro  
 275 280 285  
 Trp Gln Ala Ala Ile Phe Ala Lys His Arg Arg Ser Pro Gly Glu Arg

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290 295 300  
Phe Leu Cys Gly Gly Ile Leu Ile Ser Ser Cys Trp Ile Leu Ser Ala  
305 310 315 320  
Ala His Cys Phe Gln Glu Arg Phe Pro Pro His His Leu Thr Val Ile  
325 330 335  
Leu Gly Arg Thr Tyr Arg Val Val Pro Gly Glu Glu Glu Gln Lys Phe  
340 345 350  
Glu Val Glu Lys Tyr Ile Val His Lys Glu Phe Asp Asp Asp Thr Tyr  
355 360 365  
Asp Asn Asp Ile Ala Leu Leu Gln Leu Lys Ser Asp Ser Ser Arg Cys  
370 375 380  
Ala Gln Glu Ser Ser Val Val Arg Thr Val Cys Leu Pro Pro Ala Asp  
385 390 395 400  
Leu Gln Leu Pro Asp Trp Thr Glu Cys Glu Leu Ser Gly Tyr Gly Lys  
405 410 415  
Asp Glu Ala Leu Ser Pro Phe Tyr Ser Glu Arg Leu Lys Glu Ala His  
420 425 430  
Val Arg Leu Tyr Pro Ser Ser Arg Cys Thr Ser Gln His Leu Leu Asn  
435 440 445  
Arg Thr Val Thr Asp Asn Met Leu Cys Ala Gly Asp Thr Arg Ser Gly  
450 455 460  
Gly Pro Gln Ala Asn Leu His Asp Ala Cys Gln Gly Asp Ser Gly Gly  
465 470 475 480  
Pro Leu Val Cys Leu Asn Asp Gly Arg Met Thr Leu Val Gly Ile Ile  
485 490 495  
Ser Trp Gly Leu Gly Cys Gly Gln Lys Asp Val Pro Gly Val Tyr Thr  
500 505 510  
Lys Val Thr Asn Tyr Leu Asp Trp Ile Arg Asp Asn Met Arg Pro  
515 520 525

2) INFORMATION FOR SEQ ID NO:2:

- (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 527 amino acids  
 (B) TYPE: amino acid  
 (C) STRANDEDNESS: not relevant  
 (D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo sapiens

5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

10 Ser Tyr Gln Val Ile Cys Arg Asp Glu Lys Thr Gln Met Ile Tyr Gln  
 1 5 10 15  
 20 Gln His Gln Ser Trp Leu Arg Pro Val Leu Arg Ser Asn Arg Val Glu  
 20 25 30  
 30 Tyr Cys Trp Cys Asn Ser Gly Arg Ala Gln Cys His Ser Val Pro Val  
 35 40 45  
 40 Lys Ser Cys Ser Glu Pro Arg Cys Phe Asn Gly Gly Thr Cys Gln Gln  
 50 55 60  
 55 Ala Leu Tyr Phe Ser Asp Phe Val Cys Gln Cys Pro Glu Gly Phe Ala  
 65 70 75 80  
 60 Gly Lys Cys Cys Glu Ile Asp Thr Arg Ala Thr Cys Tyr Glu Asp Gln  
 85 90 95  
 65 Gly Ile Ser Tyr Arg Gly Thr Trp Ser Thr Ala Glu Ser Gly Ala Glu  
 100 105 110  
 70 Cys Thr Asn Trp Asn Ser Ser Ala Leu Ala Gln Lys Pro Tyr Ser Gly  
 115 120 125  
 75 Arg Arg Pro Asp Ala Ile Arg Leu Gly Leu Gly Asn His Asn Tyr Cys  
 130 135 140  
 80 Arg Asn Pro Asp Arg Asp Ser Lys Pro Trp Cys Tyr Val Phe Lys Ala  
 145 150 155 160  
 85 Gly Lys Tyr Ser Ser Glu Phe Cys Ser Thr Pro Ala Cys Ser Glu Gly  
 165 170 175  
 90 Asn Ser Asp Cys Tyr Phe Gly Asn Gly Ser Ala Tyr Arg Gly Thr His  
 180 185 190  
 95 Ser Leu Thr Glu Ser Gly Ala Ser Cys Leu Pro Trp Asn Ser Met Ile  
 195 200 205  
 100 Leu Ile Gly Lys Val Tyr Thr Ala Gln Asn Pro Ser Ala Gln Ala Leu  
 210 215 220  
 105 Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Gly Asp Ala Lys  
 225 230 235 240  
 110 Pro Trp Cys His Val Leu Lys Asn Arg Arg Leu Thr Trp Glu Tyr Cys  
 245 250 255  
 115 Asp Val Pro Ser Cys Ser Thr Cys Gly Leu Arg Gln Tyr Ser Gln Pro  
 260 265 270  
 120 Gln Phe Glu Ile Lys Gly Gly Leu Phe Ala Asp Ile Ala Ser His Pro  
 275 280 285

Trp Gln Ala Ala Ile Phe Ala Lys His Arg Arg Ser Pro Gly Glu Arg  
 290 295 300  
 Phe Leu Cys Gly Gly Ile Leu Ile Ser Ser Cys Trp Ile Leu Ser Ala  
 305 310 315 320  
 Ala His Cys Phe Gln Glu Arg Phe Pro Pro His His Leu Thr Val Ile  
 325 330 335  
 Leu Gly Arg Thr Tyr Arg Val Val Pro Gly Glu Glu Glu Gln Lys Phe  
 340 345 350  
 Glu Val Glu Lys Tyr Ile Val His Lys Glu Phe Asp Asp Asp Thr Tyr  
 355 360 365  
 Asp Asn Asp Ile Ala Leu Leu Gln Leu Lys Ser Asp Ser Ser Arg Cys  
 370 375 380  
 Ala Gln Glu Ser Ser Val Val Arg Thr Val Cys Leu Pro Pro Ala Asp  
 385 390 395 400  
 Leu Gln Leu Pro Asp Trp Thr Glu Cys Glu Leu Ser Gly Tyr Gly Lys  
 405 410 415  
 Glu Glu Ala Leu Ser Pro Phe Tyr Ser Glu Arg Leu Lys Glu Ala His  
 420 425 430  
 Val Arg Leu Tyr Pro Ser Ser Arg Cys Thr Ser Gln His Leu Leu Asn  
 435 440 445  
 Arg Thr Val Thr Asp Asn Met Leu Cys Ala Gly Asp Thr Arg Ser Gly  
 450 455 460  
 Gly Pro Gln Ala Asn Leu His Asp Ala Cys Gln Gly Asp Ser Gly Gly  
 465 470 475 480  
 Pro Leu Val Cys Leu Asn Asp Gly Arg Met Thr Leu Val Gly Ile Ile  
 485 490 495  
 Ser Trp Gly Leu Gly Cys Gly Gln Lys Asp Val Pro Gly Val Tyr Thr  
 500 505 510  
 Lys Val Thr Asn Tyr Leu Asp Trp Ile Arg Asp Asn Met Arg Pro  
 515 520 525

## 2) INFORMATION FOR SEQ ID NO:3:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 527 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: peptide

## (iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo sapiens

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

Ser	Tyr	Gln	Val	Ile	Cys	Arg	Asp	Glu	Lys	Thr	Gln	Met	Ile	Tyr	Gln
1				5					10					15	
Gln	His	Gln	Ser	Trp	Leu	Arg	Pro	Val	Leu	Arg	Ser	Asn	Arg	Val	Glu
			20					25					30		
Tyr	Cys	Trp	Cys	Asn	Ser	Gly	Arg	Ala	Gln	Cys	His	Ser	Val	Pro	Val
		35					40					45			
Lys	Ser	Cys	Ser	Glu	Pro	Arg	Cys	Phe	Asn	Gly	Gly	Thr	Cys	Gln	Gln
	50					55					60				
Ala	Leu	Tyr	Phe	Ser	Asp	Phe	Val	Cys	Gln	Cys	Pro	Glu	Gly	Phe	Ala
65					70					75					80
Gly	Lys	Cys	Cys	Glu	Ile	Asp	Thr	Arg	Ala	Thr	Cys	Tyr	Glu	Asp	Gln
				85					90					95	
Gly	Ile	Ser	Tyr	Arg	Gly	Thr	Trp	Ser	Thr	Ala	Glu	Ser	Gly	Ala	Glu
			100					105					110		
Cys	Thr	Asn	Trp	Asn	Ser	Ser	Ala	Leu	Ala	Gln	Lys	Pro	Tyr	Ser	Gly
		115					120					125			
Arg	Arg	Pro	Asp	Ala	Ile	Arg	Leu	Gly	Leu	Gly	Asn	His	Asn	Tyr	Cys
	130					135					140				
Arg	Asn	Pro	Asp	Arg	Asp	Ser	Lys	Pro	Trp	Cys	Tyr	Val	Phe	Lys	Ala
145					150					155					160
Gly	Lys	Tyr	Ser	Ser	Glu	Phe	Cys	Ser	Thr	Pro	Ala	Cys	Ser	Glu	Gly
				165					170					175	
Asn	Ser	Asp	Cys	Tyr	Phe	Gly	Asn	Gly	Ser	Ala	Tyr	Arg	Gly	Thr	His
			180					185					190		
Ser	Leu	Thr	Glu	Ser	Gly	Ala	Ser	Cys	Leu	Pro	Trp	Asn	Ser	Met	Ile
		195					200					205			
Leu	Ile	Gly	Lys	Val	Tyr	Thr	Ala	Gln	Asn	Pro	Ser	Ala	Gln	Ala	Leu
	210					215					220				
Gly	Leu	Gly	Lys	His	Asn	Tyr	Cys	Arg	Asn	Pro	Asp	Gly	Asp	Ala	Lys
225					230					235					240
Pro	Trp	Cys	His	Val	Leu	Lys	Asn	Arg	Arg	Leu	Thr	Trp	Glu	Tyr	Cys
			245					250					255		
Asp	Val	Pro	Ser	Cys	Ser	Thr	Cys	Gly	Leu	Arg	Gln	Tyr	Ser	Gln	Pro
			260					265					270		

Sequence 1300

Gln Phe Glu Ile Lys Gly Gly Leu Phe Ala Asp Ile Ala Ser His Pro  
 275 280 285  
 Trp Gln Ala Ala Ile Phe Ala Lys His Arg Arg Ser Pro Gly Glu Arg  
 290 295 300  
 Phe Leu Cys Gly Gly Ile Leu Ile Ser Ser Cys Trp Ile Leu Ser Ala  
 305 310 315 320  
 Ala His Cys Phe Gln Glu Arg Phe Pro Pro His His Leu Thr Val Ile  
 325 330 335  
 Leu Gly Arg Thr Tyr Arg Val Val Pro Gly Glu Glu Glu Gln Lys Phe  
 340 345 350  
 Glu Val Glu Lys Tyr Ile Val His Lys Glu Phe Asp Asp Asp Thr Tyr  
 355 360 365  
 Asp Asn Asp Ile Ala Leu Leu Gln Leu Lys Ser Asp Ser Ser Arg Cys  
 370 375 380  
 Ala Gln Glu Ser Ser Val Val Arg Thr Val Cys Leu Pro Pro Ala Asp  
 385 390 395 400  
 Leu Gln Leu Pro Asp Trp Thr Glu Cys Glu Leu Ser Gly Tyr Gly Lys  
 405 410 415  
 His Glu Ala Leu Ser Pro Phe Tyr Ser Glu Arg Leu Tyr Glu Ala His  
 420 425 430  
 Val Arg Leu Tyr Pro Ser Ser Arg Cys Thr Ser Gln His Leu Leu Asn  
 435 440 445  
 Arg Thr Val Thr Asp Asn Met Leu Cys Ala Gly Asp Thr Arg Ser Gly  
 450 455 460  
 Gly Pro Gln Ala Asn Leu His Asp Ala Cys Gln Gly Asp Ser Gly Gly  
 465 470 475 480  
 Pro Leu Val Cys Leu Asn Asp Gly Arg Met Thr Leu Val Gly Ile Ile  
 485 490 495  
 Ser Trp Gly Leu Gly Cys Gly Gln Lys Asp Val Pro Gly Val Tyr Thr  
 500 505 510  
 Lys Val Thr Asn Tyr Leu Asp Trp Ile Arg Asp Asn Met Arg Pro  
 515 520 525

## (2) INFORMATION FOR SEQ ID NO:4:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 290 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo sapiens

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

CTACGGCAAG	CATGAGGCCT	TGTCTCCTTT	CTATTCGGAG	CGGCTGAAGG	AGGCTCATGT	60
CAGACTGTAC	CCATCCAGCC	GCTGCACATC	ACAACATTTA	CTTAACAGAA	CAGTCACCGA	120
CAACATGCTG	TGTGCTGGAG	AACTCTGGAG	CGGCGGGCCC	CAGGCAAAC	TGCACGACGC	180
CTGCCAGGGC	GATTCGGGAG	GCCCCCTGGT	GTGTCTGAAC	GATGGCCGCA	TGACTTTGGT	240
GGGCATCATC	AGCTGGGGCC	TGGGCTGTGG	ACAGAAGGAT	GTCCCGGGTG		290

(2) INFORMATION FOR SEQ ID NO:5:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 290 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: not relevant

(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo sapiens

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

CTACGGCAAG	GACGAGGCCT	TGTCTCCTTT	CTATTCGGAG	CGGCTGAAGG	AGGCTCATGT	60
CAGACTGTAC	CCATCCAGCC	GCTGCACATC	ACAACATTTA	CTTAACAGAA	CAGTCACCGA	120
CAACATGCTG	TGTGCTGGAG	AACTCTGGAG	CGGCGGGCCC	CAGGCAAAC	TGCACGACGC	180
CTGCCAGGGC	GATTCGGGAG	GCCCCCTGGT	GTGTCTGAAC	GATGGCCGCA	TGACTTTGGT	240
GGGCATCATC	AGCTGGGGCC	TGGGCTGTGG	ACAGAAGGAT	GTCCCGGGTG		290

(2) INFORMATION FOR SEQ ID NO:6:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 290 base pairs



- (B) TYPE: nucleic acid  
(C) STRANDEDNESS: not relevant  
(D) TOPOLOGY: not relevant

- (ii) MOLECULE TYPE: cDNA  
(iii) HYPOTHETICAL: NO  
(iv) ANTI-SENSE: NO  
(vi) ORIGINAL SOURCE:  
(A) ORGANISM: Homo sapiens

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

CTACGGCAAG GAGGAGGCCT TGTCTCCTTT CTATTCGGAG CGGCTGAAGG AGGCTCATGT	60
CAGACTGTAC CCATCCAGCC GCTGCACATC ACAACATTTA CTTAACAGAA CAGTCACCGA	120
CAACATGCTG TGTGCTGGAG AACTCGGAG CGGCGGGCCC CAGGCAAAC TGCACGACGC	180
CTGCCAGGGC GATTCGGGAG GCCCCCTGGT GTGTCTGAAC GATGGCCGCA TGACTTTGGT	240
GGGCATCATC AGCTGGGGCC TGGGCTGTGG ACAGAAGGAT GTCCCGGGTG	290

(2) INFORMATION FOR SEQ ID NO:7:

- (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 290 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: not relevant  
(D) TOPOLOGY: not relevant

- (ii) MOLECULE TYPE: cDNA  
(iii) HYPOTHETICAL: NO  
(iv) ANTI-SENSE: NO  
(vi) ORIGINAL SOURCE:  
(A) ORGANISM: Homo sapiens

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

CTACGGCAAG CATGAGGCCT TGTCTCCTTT CTATTCGGAG CGGCTGTATG AGGCTCATGT	60
CAGACTGTAC CCATCCAGCC GCTGCACATC ACAACATTTA CTTAACAGAA CAGTCACCGA	120
CAACATGCTG TGTGCTGGAG AACTCGGAG CGGCGGGCCC CAGGCAAAC TGCACGACGC	180
CTGCCAGGGC GATTCGGGAG GCCCCCTGGT GTGTCTGAAC GATGGCCGCA TGACTTTGGT	240
GGGCATCATC AGCTGGGGCC TGGGCTGTGG ACAGAAGGAT GTCCCGGGTG	290

## (2) INFORMATION FOR SEQ ID NO:8:

- (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 23 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: not relevant  
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:  
(A) ORGANISM: Homo sapiens

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

CTACGGCAAG GACGAGGCCT TGT

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## (2) INFORMATION FOR SEQ ID NO:9:

- (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 23 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: not relevant  
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:  
(A) ORGANISM: Homo sapiens

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:9:

CTACGGCAAG GAGGAGGCCT TGT

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## (2) INFORMATION FOR SEQ ID NO:10:

- (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 25 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: not relevant  
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: cDNA

